

B3
cont.
SUB
C2
cont.

3 mixing cells, an alginate salt and a source of
4 calcium ions to provide a mixture;
5 adding a calcium releasing compound to the
6 mixture to provide a crosslinked hydrogel; [and]
7 selectively controlling the hydrogel system to
8 a predetermined size by varying a calcium ion
9 concentration of a medium into which the hydrogel system
10 is introduced; and
11 culturing the crosslinked [gel] hydrogel in the
12 medium to provide a three-dimensional crosslinked
13 hydrogel/cell system for growing the cells in vitro.

Please cancel claim 21 without prejudice.

B3

1 22. (Amended) The method as defined in claim
2 [21] 1 wherein the hydrogel system swelled at calcium ion
3 concentrations in the medium between about 0.0005 M and
4 about 0.0010 M; wherein the hydrogel system shrank at a
5 calcium ion concentration in the medium of about 0.0040
6 M; and wherein the hydrogel system remained substantially
7 the same size at calcium ion concentrations in the medium
8 between about 0.0020 M and about 0.0030 M.

SUB
C3

1 23. (Amended) A method for preparing a three-
2 dimensional hydrogel system, the method comprising the
3 [step] steps of:
4 adding a cation-releasing compound to a mixture
5 of at least one hydrophilic polymer and a source of
6 cations to provide a three-dimensional crosslinked
7 hydrogel system; and
8 selectively controlling the hydrogel system to
9 a predetermined size by varying a cation concentration of
10 a medium into which the hydrogel system is introduced,
11 wherein the cation in the medium is selected to be the
12 same cation as the cation in the hydrogel system.

B4
D4

1 31. (Amended) The method as defined in claim
2 24[, further comprising the step of selectively
3 controlling the hydrogel system to a predetermined size
4 by varying the calcium ion concentration] wherein the
5 cation in the medium is calcium ion.

B5

1 33. (Amended) The method as defined in claim
2 23, further comprising the step of culturing the three-
3 dimensional crosslinked hydrogel system in the medium for
4 growing cells *in vitro*.

SUB
D4

1 34. (Amended) A three-dimensional crosslinked
2 hydrogel composition, consisting essentially of:
3 at least one hydrophilic polymer;
4 a source of cations; [and]
5 a cation-releasing compound; and
6 cells incorporated into the hydrogel
7 composition, thereby forming a hydrogel/cell system.

B6

1 39. (New) The three-dimensional crosslinked
2 hydrogel composition as defined in claim 35, further
3 comprising a culture medium having a predetermined cation
4 concentration for maintaining the hydrogel/cell system.

1 40. (New) The composition as defined in claim
2 39 wherein the predetermined cation concentration is a
3 calcium ion concentration between about 0.0020 M and
4 about 0.0030 M.

SUB
C5

1 41. (New) The composition as defined in claim
2 34 wherein the cells are at least one of osteoblasts and
3 cells which secrete a medically useful compound.

1 42. (New) The method of claim 2 wherein the
2 cells secrete a medically useful compound.

1 43. (New) The method of claim 11 wherein the
2 cells secrete a medically useful compound.

1 44. (New) The method of claim 33 wherein the
2 cells are at least one of osteoblasts and cells which
3 secrete a medically useful compound.

REMARKS

The Office Action of September 11, 2000 has been received and carefully reviewed. It is submitted that, by this Amendment, all bases of rejection and objection are traversed and overcome. Upon entry of this Amendment, Claims 1-20 and 22-38 remain in the application. New claims 39-44 have been added in order to set forth specific additional embodiments of Applicant's invention.

Claims 1, 3-7, 9, 23-28 and 33-36 stand rejected under 35 U.S.C. 102(e) as being anticipated by Draget et al (1991). The Examiner stated that Applicant's claimed invention is to a product and a method of making in vitro, consisting essentially of a sodium alginate salt, or alginate derived from *Macrocystis pyrifera* or *Laminaria hyperborea*, calcium carbonate and GDL, wherein the ratio of calcium carbonate to GDL is 0.5, and the thickness is between 4-8 mm and the diameter is approximately 18 mm.

The Examiner further stated that Draget teaches the formation of a gel consisting of mixing 15 mM CaCO_3 with sodium alginate solution, then adding 30 mM GDL, resulting in a final gel of pH 7. The Examiner further stated that Draget teaches that the sodium alginate can be substituted with alginate derived from *Macrocystis pyrifera* or *Laminaria hyperborea*, thus altering the viscosity of the gel, and that the dimensions of the gel are largely a function of the dimensions of the mold into which they form, and can thus be easily modified by one of ordinary skill in the art. Therefore, the Examiner